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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/393,023	09/09/1999	PAUL S. MEISSNER	PF-200	2146

22195 7590 11/26/2001

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EXAMINER
KAUFMAN, CLAIRE M

ART UNIT	PAPER NUMBER
1646	17

DATE MAILED: 11/26/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/393,023	Applicant(s) MEISSNER ET AL.	
	Examiner Claire M. Kaufman	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09/09/99, 12/08/99, 05/17/01* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,16 and 19-95* is/are pending in the application.

4a) Of the above claim(s) *14,16,19,20,22-25,27-32,34 and 38-95* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,26,33 and 35-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *14,16 and 19-95* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 September 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 11.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendments filed 9/9/99, 12/8/99 and 5/17/01 have been entered.

Election/Restrictions

Applicant's election with traverse of Group I of protein comprising amino acids 24-173 of SEQ ID NO:2 in Paper No. 16 is acknowledged. The traversal is on the ground(s) that 1) this should be/is a species election with additional species being examined if the first species is found allowable, 2) there is no serious burden of search for examining multiple sequences. This is not found persuasive.

With respect to Applicants' first point, although the word "species" was used in the restriction of 7/6/01, it was not a "species" restriction/election. Each embodiment set forth in the restriction is a distinct and separate invention. There is no generic claim since art against a fragment would not constitute art against the full-length protein, and the art against one fragment would not necessarily constitute art against another. As a result, only one invention will be examined: a protein comprising amino acids 24-173 of SEQ ID NO:2.

With respect to Applicants' second point, there is a serious burden of search for searching the multiple sequences/proteins claimed. Some fragments are short and need to be only 90% identical to a disclosed fragment, so the sequence could be embedded within other patentably distinct proteins. Therefore, it cannot be said that they are merely fragments of a common protein. A separate search is required for each possible fragment. Searching the full-length protein sequence will not necessarily result in the identification of art pertinent to the fragments since the USPTO search system generally has a limited number of "hits" saved and the burden of search for the Office has increased with multiple sequences because of the rapid introduction of new sequences to public sequence databases.

The requirement is still deemed proper and is therefore made FINAL.

The elected invention is a protein comprising a polypeptide having an amino acid sequence of residues 24-173 of SEQ ID NO: 2. Thus, claims 21, 26, 33 and 35-37 as they are

drawn to the elected invention are under consideration. Claims 14, 16, 19, 20, 22-25, 27-32, 34 and 38-95 are withdrawn from prosecution as being drawn to a non-elected invention.

Drawings

The corrected or substitute drawings were received on 12/8/99. These drawings are approved.

Response to Amendment

The Declaration under 37 CFR 1.132 filed 12/8/99 is sufficient to address potential issues of new matter relating to the sequence differences between this and the parent application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21, 26, 33 and 35-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 32 of U.S. Patent No. 5,981,215. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claims encompass the protein encoded by the cDNA clone contained in ATCC No. 97142. Further, it would have been obvious to express the cDNA in a host cell, recovering the protein which can be glycosylated depending on the type of host cell. Such a protein is generally recovered in a buffer, a pharmaceutically acceptable carrier. It further would have been obvious for the protein to further comprise a heterologous polypeptide

which functioned as a purification tag, for example, because it was well known that the many commercially available protein purification tags were valuable tools at the time the instant invention was made (see also claim 42 and 47 of US Patent No. 5,981,215).

Claim Objections

Claims 21, 33 and 35-37 are objected to for encompassing multiple patentably distinct inventions. The claims should be amended to include only the elected invention. Correction is required.

Objections and Rejections under 35 U.S.C. §§101 and 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 21, 26, 33 and 35-37 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility.

The utility set forth in the specification p.17, last paragraph, is that of pancreatic cancer diagnosis. This is based on "An initial Northern blot analysis [that] has shown very high expression in pancreatic cancer cells." For several reasons this is not a specific or substantial utility. First, it is not know how the level of expression compares to expression in normal noncancerous cells, nor if the expression was analyzed in cell cultures or in cancerous tissue. Markers for cell lines are not necessarily representative of primary cell cultures or tissue since it is well known that cells can undergo changes in expression when cultured for extended passages. Also, a cancer cell line is representative of only a single sample (cell lines originate from 1 patient's cells), which is not enough information to conclude that protein alteration in that cell line is a universal phenomenon in all or most pancreatic cell samples. Second, polynucleotide expression is not necessarily indicative of protein expression. There is no information on altered level of protein (the claimed product) in pancreatic cancer cells.

The specification teaches that the mature criptin protein (amino acids 24-223 of SEQ ID NO:2) has the putative activity of wound healing and stimulation of vasculogenesis (p. 18,3rd and 4thfull paragraph). The prior art teaches a structurally related protein called "cripto" which has been identified as a cancer marker (p. 2, third paragraph; and references AA and AE), as well as a related gene called "CR-3" (AB), the function of which is also unknown. Neither of these prior art proteins is disclosed as having a transmembrane domain, although criptin is disclosed as having a transmembrane domain (p. 4, 8 lines from bottom). In the current instance the nature the invention is largely unknown since the related prior art proteins have no described function except as tumor cell markers and have a conserved "EGF motif" which confers some structural form. There are no examples of criptin promoting would healing or vasculogenesis. The list of tissue in which it may promote would healing is diverse: skin, bone, muscle, lung..., and no specific tissue is identified nor under what circumstances criptin can actually promote wound healing (*e.g.*, cellular state of tissue--proliferating or differentiating, effective amount, or *in vivo* compared to *in vitro* activity). Also, the currently claimed protein has several putative functions listed and a putative three dimensional structure, but without information on the relationship of structure to function.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 26, 33 and 35-37 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the means by which the protein can be produced. There s nothing to indicate the host cell anything by which it can produce the protein, for example, a nucleic acid encoding the protein.

Claim 37 is indefinite because in step (b), it is unclear if "the protein" recovered is said isolated protein of claim 21 or if it is another protein in/from the cell.

Claim 34 is indefinite for failing to indicate the relationship between the recited structural elements. Specifically, it is not clear how the "heterologous polynucleotide" of claim 34, for example, relates to the polynucleotide of claim 21. In claim 34, it is not clear whether the heterologous sequence is attached at an end or might be internally inserted.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

November 15, 2001